

Citation for published version:

Yates, C & Chappelle, G 2019, 'Pulling in models of cell migration', *Physical Review E*, vol. 99, no. 6, 062413, pp. 1-35. <https://doi.org/10.1103/PhysRevE.99.062413>

DOI:

[10.1103/PhysRevE.99.062413](https://doi.org/10.1103/PhysRevE.99.062413)

Publication date:

2019

Document Version

Peer reviewed version

[Link to publication](https://doi.org/10.1103/PhysRevE.99.062413)

Copyright © 2019 American Physical Society. The final publication is available at PHYSICAL REVIEW E via <https://doi.org/10.1103/PhysRevE.99.062413>

University of Bath

Alternative formats

If you require this document in an alternative format, please contact:
openaccess@bath.ac.uk

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Supplementary material to accompany: Pulling in models of cell migration

George Chappelle

Department of Mathematics, Imperial College London, SW7 2AZ, UK

Christian A. Yates*

Centre for Mathematical Biology, Department of Mathematical Sciences,

University of Bath, Claverton Down, Bath, BA2 7AY, UK

(Dated: April 2, 2019)

* Corresponding Author: c.yates@bath.ac.uk; Website: <http://people.bath.ac.uk/cy386/>

This supplementary materials document is broken down into two sections. In Section S1 we present a range of mean occupancy equations for the various on and off-lattice pulling models specified in the main text. The interested reader may then employ method of derivation supplied in the main text in order to rederive the partial differential equations (PDEs) supplied in the main text if desired. In Section S2 we present the derivation of the PDE from the off-lattice agent-based model of contact forming described in Subsection IV B of the main text.

S1. ADDITIONAL OCCUPANCY EQUATIONS

In this section we present the mean-occupancy equations which were omitted from the main text. All mean-occupancy equations are presented in 1-D for simplicity and consistency.

A. Pushing

This is the average-occupancy equation for the pushing model mentioned in Section II C of the main text and derived in [?]]

$$\begin{aligned}
C(i, t + \delta t) - C(i, t) = & \\
& - \frac{p}{2} C(i, t) \left[(1 - C(i + 1, t)) + (1 - C(i - 1, t)) \right. \\
& + q \left\{ C(i + 1, t)(1 - C(i + 2, t)) + C(i - 1, t)(1 - C(i - 2, t)) \right\} \left. \right] \delta t \\
& + \frac{p}{2} (1 - C(i, t)) \left[C(i + 1, t) + C(i - 1, t) \right. \\
& + q \left\{ C(i + 1, t)C(i + 2, t) + C(i - 1, t)C(i - 2, t) \right\} \left. \right] \delta t.
\end{aligned} \tag{S1}$$

B. Type 1 multiple pulling

This is the mean-occupancy equation for the type 1 second-order pulling model in Section III A of the main text:

$$\begin{aligned}
C(i, t + \delta t) - C(i, t) = & \\
& - \frac{p}{2} C(i, t) \left[(2(1 - C(i - 1, t))(1 - C(i + 1, t)) + w \left\{ (C(i + 1, t)(1 - C(i + 2, t))(1 - w_1 C(i - 1, t)) \right. \right. \right.
\end{aligned}$$

$$\begin{aligned}
& + C(i-1, t)(1 - C(i-2, t))(1 - w_1 C(i+1, t)) \Big\} \\
& + (1 - w) \Big\{ (C(i-1, t)(1 - C(i+1, t)) + C(i+1, t)(1 - C(i-1, t))) \Big\} \\
& + ww_1 \Big\{ C(i+1, t)C(i+2, t)(1 - C(i+3, t)) + C(i-1, t)C(i-2, t)(1 - C(i-3, t)) \Big\} \Big] \delta t \\
& + \frac{p}{2} (1 - C(i, t)) \Big[C(i-1, t) + C(i+1, t) \Big] \delta t. \tag{S2}
\end{aligned}$$

C. Type 2 multiple pulling

This is the mean-occupancy equation for the type 2 second-order pulling model in Section III A of the main text:

$$\begin{aligned}
C(i, t + \delta t) - C(i, t) = & - \frac{p}{2} C(i, t) \Big[2(1 - C(i-1, t))(1 - C(i+1, t)) \\
& + r_1 \Big\{ C(i+1, t)(1 - C(i+2, t)) + C(i-1, t)(1 - C(i-2, t)) \Big\} \\
& + (1 - r_1) \Big\{ C(i-1, t)(1 - C(i+1, t))(1 - r_2 C(i-2)) + C(i+1, t)(1 - C(i-1, t))(1 - r_2 C(i+2)) \\
& + r_2 \Big(C(i+1, t)C(i+2, t)(1 - C(i+3, t)) + C(i-1, t)C(i-2, t)(1 - C(i-3, t)) \Big) \Big\} \Big] \delta t \\
& + \frac{p}{2} (1 - C(i, t)) \Big[C(i-1, t) + C(i+1, t) \Big] \delta t. \tag{S3}
\end{aligned}$$

D. Pulling and pushing

This is the mean-occupancy equation for the model combining pushing and pulling in Section III B of the main text:

$$\begin{aligned}
C(i, t + \delta t) - C(i, t) = & - \frac{p}{2} C(i, t) \Big[(1 - C(i+1, t))(1 - wC(i-1, t)) + (1 - C(i-1, t))(1 - wC(i+1, t)) \\
& + C(i+1, t)(1 - C(i+2, t)) \Big\{ (1 - C(i-1, t))w + C(i-1, t)w(1 - q) + q \Big\} \\
& + C(i-1, t)(1 - C(i-2, t)) \Big\{ (1 - C(i+1, t))w + C(i+1, t)w(1 - q) + q \Big\} \\
& + C(i+1, t)C(i+2, t)(1 - C(i+3, t))qw + C(i-1, t)C(i-2, t)(1 - C(i-3, t))qw \Big] \delta t \\
& + \frac{p}{2} (1 - C(i, t)) \Big[C(i+1, t)(1 + C(i+2, t)w) + C(i-1, t)(1 + C(i-2, t)w) \Big] \delta t. \tag{S4}
\end{aligned}$$

E. Pulling at a distance

This is the mean-occupancy equation for the pulling at a distance model in Section III C of the main text:

$$\begin{aligned}
C(i, t + \delta t) - C(i, t) = & \\
& - \frac{p}{2} C(i, t) \left[(1 - C(i + 1, t)) \{ (1 - C(i - 1, t)) + (1 - w) C(i - 1, t) \} + w C(i + 1, t) (1 - C(i + 2, t)) \right. \\
& + w (1 - C(i + 1, t)) C(i + 2, t) (1 - C(i + 1, t)) \\
& + (1 - C(i - 1, t)) \{ (1 - C(i + 1, t)) + (1 - w) C(i + 1, t) \} \\
& + w C(i - 1, t) (1 - C(i - 2, t)) + w (1 - C(i - 1, t)) C(i - 2, t) (1 - C(i - 3, t)) \left. \right] \delta t \\
& + \frac{p}{2} (1 - C(i, t)) \left[C(i + 1, t) \{ 1 + w C(i - 1, t) (1 - C(i - 2, t)) \} \right. \\
& + C(i - 1, t) \{ 1 + w C(i + 1, t) (1 - C(i + 2, t)) \} \left. \right] \delta t. \tag{S5}
\end{aligned}$$

F. Off-lattice pulling at a distance

This is the mean-occupancy equation for the off-lattice pulling-at-a-distance model in Section IV C of the main text

$$\begin{aligned}
C_i(x, t + dt) - C_i(x) = & \frac{pdt}{2} C_i(x - d) \left(1 - \sum_{j \neq i} \int_{2R}^{2R+d} C_i(x - d + s) ds \right) \\
& + \frac{pdt}{2} C_i(x + d) \left(1 - \sum_{j \neq i} \int_{-2R-d}^{-2R} C_i(x + d + s) ds \right) \\
& - \frac{pdt}{2} C_i(x) \left(1 - \sum_{j \neq i} \int_{2R}^{2R+d} C_i(x + s) ds \right) \\
& - \frac{pdt}{2} C_i(x) \left(1 - \sum_{j \neq i} \int_{-2R-d}^{-2R} C_i(x + s) ds \right) \\
& + \frac{Qpdt}{2} C_i(x - d) \sum_{j \neq i} \int_{2R}^{2R+dk} C_j(x - d + s) \left(1 - \sum_{k \neq i, j} \int_{2R+s}^{2R+s+d} C_k(x - d + S) dS \right) ds \\
& + \frac{Qpdt}{2} C_i(x + d) \sum_{j \neq i} \int_{-2R-dk}^{-2R} C_j(x + d + s) \left(1 - \sum_{k \neq i, j} \int_{-2R-s-d}^{-2R-s} C_k(x + d + S) dS \right) ds \\
& - \frac{Qpdt}{2} C_i(x) \sum_{j \neq i} \int_{2R}^{2R+dk} C_j(x + s) \left(1 - \sum_{k \neq i, j} \int_{2R+s}^{2R+s+d} C_k(x + S) dS \right) ds
\end{aligned}$$

$$- \frac{Qpdt}{2} C_i(x) \sum_{j \neq i} \int_{-2R-dk}^{-2R} C_j(x+s) \left(1 - \sum_{k \neq i,j} \int_{-2R-s-d}^{-2R-s} C_k(x+S) dS \right) ds. \quad (\text{S6})$$

The first four terms are the same as equation (9) of the main text. The additional four terms describe the pulling at a distance mechanism. The fifth and sixth terms describe gaining occupancy by agent i being pulled into position x . The seventh and eight terms represent losing occupancy as agent i is pulled out of position x by a nearby agent.

S2. CONTACT FORMING MODEL PDE DERIVATION

We can now derive a corresponding PDE, in the same manner as we did in section IV A of the main text. First we re-arrange equation (21) of the main text and take the limit as $dt \rightarrow 0$ to obtain a time derivative on the left hand side. Then we Taylor expand the density terms around x . For brevity, we write $C_i := C_i(x)$ in what follows:

$$\begin{aligned} \frac{\partial C_i}{\partial t} = & -\frac{\alpha}{2} C_i \left(2 - \sum_{j \neq i} C_j(x-2R) - \sum_{j \neq i} C_j(x+2R) \right) \\ & + \frac{\alpha}{2} \left[C_i - d \frac{\partial C_i}{\partial x} + \frac{d^2}{2} \frac{\partial^2 C_i}{\partial x^2} \right] (1 - P_r^i(x-d)) \\ & + \frac{\alpha}{2} \left[C_i + d \frac{\partial C_i}{\partial x} + \frac{d^2}{2} \frac{\partial^2 C_i}{\partial x^2} \right] (1 - P_l^i(x+d)) \\ & + \frac{\alpha}{2} \left[d C_i - \frac{d^2}{2} \frac{\partial C_i}{\partial x} + \frac{d^3}{6} \frac{\partial^2 C_i}{\partial x^2} \right] \sum_{j \neq i} C_j(x+2R) \\ & + \frac{\alpha}{2} \left[d C_i + \frac{d^2}{2} \frac{\partial C_i}{\partial x} + \frac{d^3}{6} \frac{\partial^2 C_i}{\partial x^2} \right] \sum_{j \neq i} C_j(x-2R) \\ & - \frac{\alpha}{2} C_i \left(\sum_{j \neq i} C_j(x+2R) + \sum_{j \neq i} C_j(x-2R) \right). \end{aligned}$$

Rearranging gives

$$\frac{\partial C_i}{\partial t} = \frac{\alpha}{2} C_i \left(d \left(\sum_{j \neq i} C_j(x-2R) + \sum_{j \neq i} C_j(x+2R) \right) - P_r^i(x-d) - P_l^i(x+d) \right) \quad (\text{S7})$$

$$+ \frac{\alpha d}{2} \frac{\partial C_i}{\partial x} \left(P_r^i(x-d) - P_l^i(x+d) + \frac{d}{2} \left(\sum_{j \neq i} C_j(x-2R) - \sum_{j \neq i} C_j(x+2R) \right) \right) \quad (\text{S8})$$

$$+ \frac{\alpha d^2}{4} \frac{\partial^2 C_i}{\partial x^2} \left(2 - P_r^i(x-d) - P_l^i(x+d) + \frac{d}{3} \left(\sum_{j \neq i} C_j(x+2R) + \sum_{j \neq i} C_j(x-2R) \right) \right). \quad (\text{S9})$$

Taylor expanding the entire equation becomes extremely cumbersome so we analyse the coefficients of C_i , $\frac{\partial C_i}{\partial x}$ and $\frac{\partial^2 C_i}{\partial x^2}$ individually before recombining later. First we simplify the coefficient of C_i in equation (S9) by Taylor expanding $C_j(x+2R)$ and $C_j(x-2R)$ around x to give

$$\begin{aligned} & d \left(\sum_{j \neq i} C_j(x-2R) + \sum_{j \neq i} C_j(x+2R) \right) - P_r^i(x-d) - P_l^i(x+d) \\ &= d \left(2 \sum_{j \neq i} C_j + 4R^2 \sum_{j \neq i} \frac{\partial^2 C_j}{\partial x^2} \right) - 2d \sum_{j \neq i} C_j - \frac{d}{3} (12R^2 + 6Rd + d^2) \sum_{j \neq i} \frac{\partial^2 C_i}{\partial x^2} \\ &= \left(2Rd^2 - \frac{d^3}{3} \right) \sum_{j \neq i} \frac{\partial^2 C_j}{\partial x^2}. \end{aligned} \quad (\text{S10})$$

Next we simplify the coefficient of $\frac{\partial C_i}{\partial x}$ in equation (S9):

$$\begin{aligned} & P_r^i(x-d) - P_l^i(x+d) + \frac{d}{2} \left(\sum_{j \neq i} C_j(x-2R) - \sum_{j \neq i} C_j(x+2R) \right) \\ &= d(4R-d) \sum_{j \neq i} \frac{\partial C_j}{\partial x} - 2Rd \sum_{j \neq i} \frac{\partial C_j}{\partial x} \\ &= (2Rd - d^2) \sum_{j \neq i} \frac{\partial C_j}{\partial x}. \end{aligned} \quad (\text{S11})$$

Finally, we can simplify the coefficient of $\frac{\partial^2 C_i}{\partial x^2}$ in (S9). We neglect terms which include an expression for $R^a d^b$ whenever $a+b > 3$, to give

$$\begin{aligned} & 2 - P_r^i(x-d) - P_l^i(x+d) + \frac{d}{3} \left(\sum_{j \neq i} C_j(x+2R) + \sum_{j \neq i} C_j(x-2R) \right) \\ & \approx 2 - 2d \sum_{j \neq i} C_j + \frac{2d}{3} \sum_{j \neq i} C_j + \frac{2d}{3} 4R^2 \sum_{j \neq i} \frac{\partial^2 C_j}{\partial x^2} \\ &= 2 - \frac{4d}{3} \sum_{j \neq i} C_j. \end{aligned} \quad (\text{S12})$$

Substituting the coefficients of C_i , $\frac{\partial C_i}{\partial x}$ and $\frac{\partial^2 C_i}{\partial x^2}$ from equations (S10), (S11) and (S12) respectively into equation (S9) gives the PDE

$$\frac{\partial C_i}{\partial t} = \frac{\alpha}{2} C_i \left[\left(2Rd^2 - \frac{d^3}{3} \right) \sum_{j \neq i} \frac{\partial^2 C_j}{\partial x^2} \right] + \frac{\alpha d}{2} \frac{\partial C_i}{\partial x} \left[(2Rd - d^2) \sum_{j \neq i} \frac{\partial C_j}{\partial x} \right] + \frac{\alpha d^2}{4} \frac{\partial^2 C_i}{\partial x^2} \left[2 - \frac{4d}{3} \sum_{j \neq i} C_j \right].$$

Assuming all agents are initialised with the same distribution, $C_i = C_j$ for all i, j and obey the same rules, we can assume $\sum_{j \neq i} C_j = (N - 1)C_i$. Consequently, we obtain

$$\frac{\partial C_i}{\partial t} = \frac{\alpha d^2}{2} \frac{\partial^2 C_i}{\partial x^2} + \frac{\alpha(N - 1)}{2} \left[(2Rd^2 - d^3) C_i \frac{\partial^2 C_i}{\partial x^2} + (2Rd^2 - d^3) \left(\frac{\partial C_i}{\partial x} \right)^2 \right].$$

We can write this in conservative form as follows

$$\frac{\partial C_i}{\partial t} = \frac{\alpha d^2}{2} \frac{\partial}{\partial x} \left(\left(1 + (N - 1)(2R - d)C_i \right) \frac{\partial C_i}{\partial x} \right). \quad (\text{S13})$$

□ C.A. Yates, A. Parker, and R.E. Baker. Incorporating pushing in exclusion-process models of cell migration. *Phys. Rev. E*, 91(5):052711, 2015.